DOI: 10.7860/JCDR/2024/72578.19843

Case Series

Dermatology Section

Atypical Manifestations of Syphilis: A Case Series

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ABSTRACT

Syphilis is a sexually transmitted disease with a wide range of clinical manifestations. Given the recent worldwide resurgence of syphilis, it is imperative to recognise various presentations of this great imitator. Apart from the classic ulcerative lesion of primary syphilis, known as a hard chancre, atypical presentations mimicking other diseases are also reported. A patient with carcinoma of the lip who was scheduled for surgery was diagnosed with an extragenital chancre during routine presurgery screening, leading to a change in the treatment plan for the patient. Other patients were initially treated for conditions such as scrotal eczema, psoriasis, and herpes before the correct diagnosis was made. Rare presentations, such as pustular lesions, paraphimosis, and cord-like thickening of the penis, were also observed in this case series. It is important to recognise these atypical manifestations, as doing so may facilitate early diagnosis and prompt management. Nine cases of syphilis in patients who exhibited atypical manifestations are presented in this case series and were diagnosed based on a high index of suspicion aided by laboratory confirmation.

Keywords: Genital ulcers, Sexually transmitted disease, Self-medication, *Treponema pallidum*

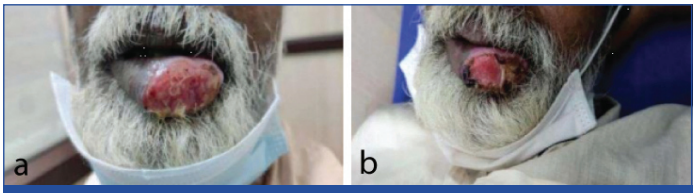
INTRODUCTION

Syphilis is a sexually transmitted infection caused by the Spirochaete bacterium *Treponema pallidum*, which has long been recognised for its varied clinical presentations. The disease is notable for its complex natural history, involving distinct clinical stages that can present with a wide array of symptoms, often mimicking other medical conditions and leading to diagnostic challenges [1]. Despite significant advances in medical science, syphilis remains a major public health challenge worldwide. Traditionally, the disease progresses through well-defined stages: primary, secondary, latent, and tertiary. Each stage is characterised by a distinct set of symptoms, ranging from the painless chancre of primary syphilis to the more severe neurological and cardiovascular complications of tertiary syphilis [1,2]. However, the symptoms can vary widely in presentation and severity, often mimicking other diseases and leading to potential misdiagnosis. Syphilis poses a unique challenge due to its ability to present with atypical manifestations, making clinical suspicion and accurate diagnosis critical. The resurgence of syphilis in many parts of the world, particularly among certain high-risk populations, underscores the need for continued vigilance and awareness among healthcare providers. This is compounded by the fact that syphilis can significantly increase the risk of Human Immunodeficiency Virus (HIV) transmission and acquisition, further complicating its impact on public health [3]. These unusual manifestations can occur at any stage of the disease and often lead to misdiagnosis. They may involve various organ systems, presenting as dermatological, ophthalmological, neurological, or even systemic symptoms that do not conform to the classic descriptions. Atypical manifestations like extragenital chancre, Follmann balanitis, scrotal eczema, and cord-like thickening in the penis are also reported. With the recent worldwide resurgence of syphilis [1,2], it is imperative to recognise these atypical manifestations promptly to prevent delays in treatment and curb potential spread in the community. In this case series, nine patients with varied atypical manifestations of syphilis have been reported.

CASE SERIES

Case 1

Ulcer of lip mimicking squamous cell carcinoma: A 57-year-old male with a diagnosis of squamous cell carcinoma of the lip was referred for presurgical HIV screening [Table/Fig-1a]. Physical examination revealed a painless, indurated ulcer on the lower lip, accompanied by non tender unilateral cervical lymphadenopathy of four weeks duration. His sexual history indicated multiple unprotected homosexual contacts over the past 35 years, engaging in both anoinsertive, anoreceptive roles, and oral sex. His last contact was seven weeks ago. He had a history of applying topical native medication, but the details were unavailable. As a routine screening for Rapid Plasma Reagin (RPR), *Treponema pallidum* Hemagglutination Assay (TPHA), and HIV was done, serological tests showed a RPR titer of 1:64 and a positive TPHA, indicating syphilis infection. However, his HIV screening result was non reactive. Based on the above details, a diagnosis of extragenital chancre was made, and the patient was treated with injection benzathine penicillin 2.4 million units [Table/Fig-1b]. The lesion healed well in three weeks, and the RPR titre was 1:4 at four weeks after treatment.

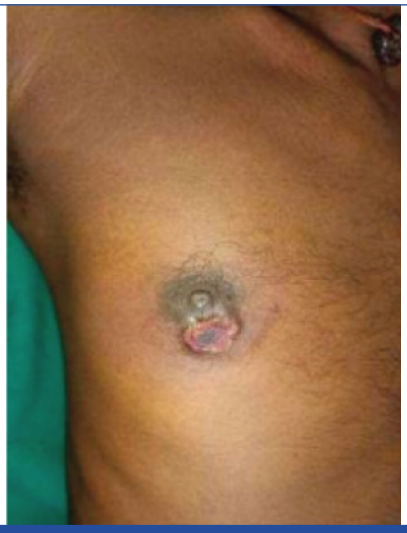


[Table/Fig-1]: a) Ulcer of lip mimicking squamous cell carcinoma;. b) After injection Benzathine penicillin.

Case 2

Crusted ulcer on areola mimicking ecthyma: A 25-year-old male presented with a complaint of ulceration over the nipple for three days [Table/Fig-2]. The patient was referred from the Dermatology outpatient clinic for screening because of his sexual history and non healing, non tender ulcer. The ulcer started as a small raised lesion three weeks ago and gradually increased in size, eventually ulcerating. Physical examination revealed a painless, non indurated ulcer on the nipple, accompanied by a few firm, non tender axillary lymphadenopathy. His contact history indicated multiple unprotected homosexual activities over the past two years, with a receptive role. He also reported a history of topical self-medication, details of which were unavailable. Serological tests showed an RPR titer of 1:16 and a positive TPHA, indicative of syphilis infection.

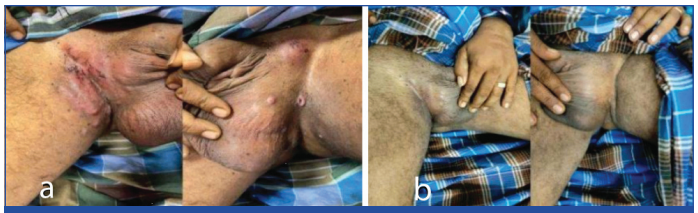
However, his HIV screening result was non reactive. He was treated with injection benzathine penicillin 2.4 mega units. The lesion healed well, and the RPR titer was 1:8 after four weeks.



[Table/Fig-2]: Crusted ulcer on areola mimicking ecthyma.

Case 3

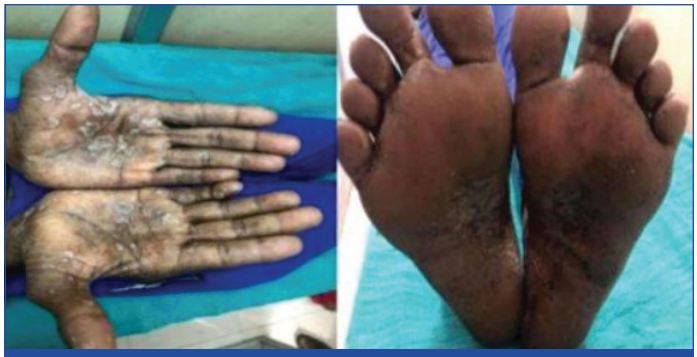
Mutiple nodules and sinuses in groin mimicking lymphadenitis with sinus: A 42-year-old male presented with painful lesions and discharge over the groin for 15 days [Table/Fig-3a]. Physical examination revealed painful erythematous plaques with nodules, some of which had ruptured to form sinuses with pus discharge. Upon questioning, he reported a history of unprotected heterosexual contacts with multiple unknown partners for the past 20 years, with the last contact being five weeks ago. He developed boil-like lesions and received treatment at a nearby hospital with systemic medications, although the details were not known. However, the lesions did not heal, and over the last two weeks, they progressed to painful ulcers and nodules, prompting him to visit Sexually Transmitted Disease (STD) outpatient clinic. Hidradenitis was considered as a possible differential diagnosis. Serological tests showed an RPR titer of 1:2 and a positive TPHA, indicating syphilis infection. However, his HIV screening result was non reactive. An injection benzathine penicillin 2.4 mega unit was given [Table/Fig-3b]. Lesions healed completely in four weeks, and the RPR titer became non reactive at six weeks.



[Table/Fig-3]: a) Mutiple nodules and sinuses in groin mimicking lymphadenitis with sinus. b) One month after single dose of penicillin.

Case 4

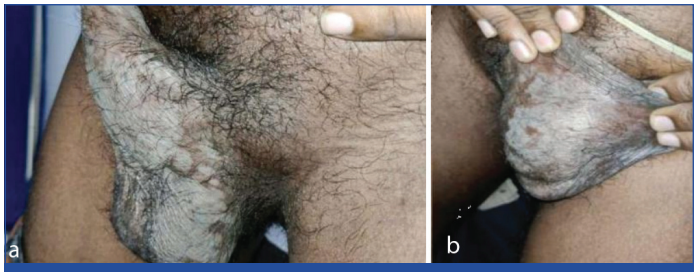
Hyperkeratotic scaly plaques resembling psoriasis: A 28-year-old male presented with lesions over the palms and soles, characterised by multiple hyperkeratotic plaques [Table/Fig-4]. He had been previously diagnosed and treated for palmoplantar psoriasis at a private clinic by a general practitioner with mometasone and salicylic acid ointment, without resolution of the lesions. His sexual history revealed that he had homosexual contacts over the past seven years, engaging in both receptive and insertive roles. Serological tests revealed an RPR titer of 1:128 and a positive TPHA, indicative of syphilis infection. Additionally, his HIV screening result was reactive. He was treated with three doses of injection benzathine penicillin 2.4 mega units due to his HIV status and was also started on Antiretroviral Therapy (ART). The lesions healed in eight weeks. After 12 weeks, RPR was 1:4.



[Table/Fig-4]: Hyperkeratotic scaly plaques resembling psoriasis.

Case 5

Scrotal eczema: A 37-year-old male presented with scaly lesions persisting on the scrotum for three months [Table/Fig-5a]. The patient first developed mild itching and scaling over the groin folds, which later progressed to involve the scrotum and penile shaft symmetrically. There was no significant past history of genital lesions or STD treatment. Physical examination revealed multiple geographic scaly plaques on the scrotum and shaft of the penis. The patient had been treated for scrotal eczema in a private clinic with medications, moisturisers, and topical clobetasol application. He reported sexual contact with unknown partners over the past 17 years. Serological tests revealed an RPR titer of 1:8 and a positive TPHA indicative of syphilis infection. Additionally, his HIV serology was reactive. He was treated with three doses of injection benzathine penicillin 2.4 mega units because of his HIV status. Topical emollients and antihistamines were also given. The patient responded well, and within a week, the lesions started to heal [Table/Fig-5b]. Complete healing was achieved by six weeks, and the RPR titer decreased to 1:2 at eight weeks.



[Table/Fig-5]: a) Scrotal eczema. b) Two weeks after Inj. Benzathine penicillin.

Case 6

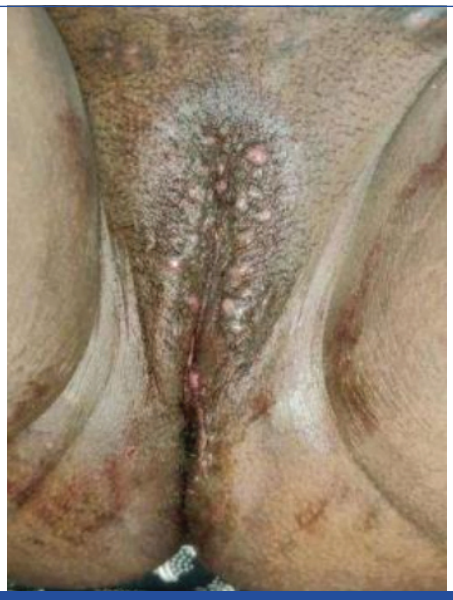
Non indurated annular plaques resembling genital psoriasis/ lichen planus: A 26-year-old male presented with raised lesions over the penis persisting for 15 days [Table/Fig-6]. Physical examination revealed multiple non tender annular plaques over the shaft of the penis and scrotum, with no similar lesions observed elsewhere on the body. Initially, the diagnosis of genital psoriasis or lichen planus was considered. Upon inquiring about his sexual history, he reported multiple unprotected homosexual activities over the past four years, with an insertive role. Serological tests showed an RPR titer of 1:32 and a positive TPHA, indicating syphilis infection. However, his HIV serology was non reactive. He was treated with benzathine penicillin 2.4 million units, and the lesions subsided by four weeks. The RPR titer was 1:4 after 12 weeks.

Case 7

Multiple painful superficial ulcers- Herpes genitalis: A 24-year-old married female presented with multiple painful ulcerations over the genitalia persisting for seven days [Table/Fig-7]. There was no history of vesicles. The patient was treated with Acyclovir by a gynaecologist, but the lesions did not heal and also increased in size and number. Tests, including Tzanck smear and Herpes Simplex Virus (HSV) serology, were negative for HSV infection. The patient denied both extramarital and premarital sexual contact. However,

serological tests revealed an RPR titer of 1:32 and a positive TPHA, indicating syphilis infection. Additionally, her HIV serology was reactive. Subsequent partner screening confirmed both syphilis and HIV positivity in her husband, who did not exhibit any genital or skin lesions. Both individuals were treated with three doses of injection benzathine penicillin 2.4 million units. Pain subsided, and the lesions healed well over a period of 12 days.

[Table/Fig-6]: Non indurated annular plaques resembling genital psoriasis/lichen planus.



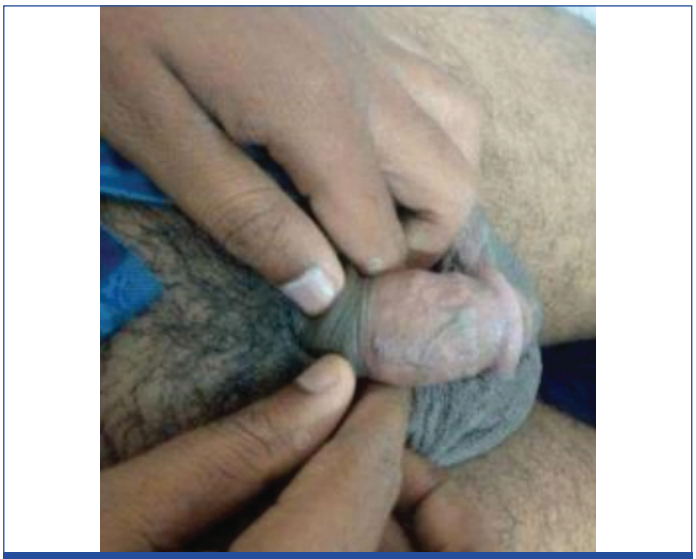
[Table/Fig-7]: Multiple painful superficial ulcers-herpetic.

Case 8

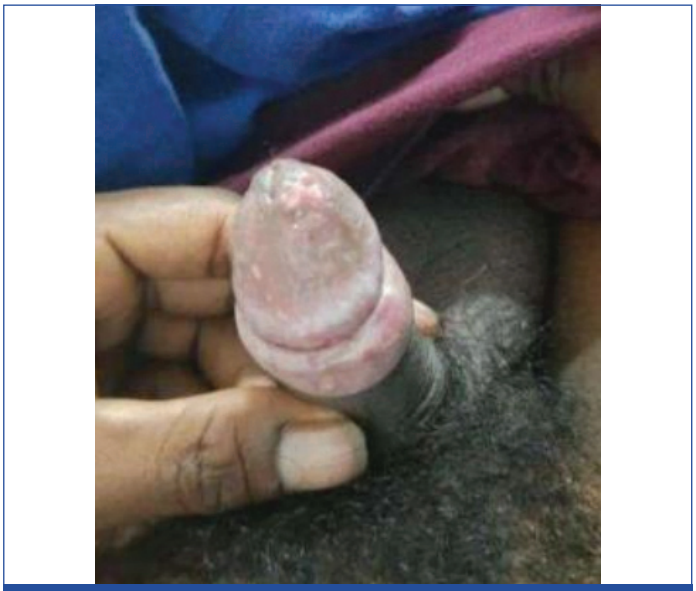
Cord like thickening: A 25-year-old male presented with a lesion over the penis associated with slight discomfort during erection [Table/Fig-8]. He had no significant past medical history of urethral discharge or genital ulcerations. Examination revealed a painless cord-like thickening measuring 0.5×4 cm over the dorsal aspect of the penis. Upon inquiring about his contact history, he reported multiple unprotected homosexual activities over the past four years, primarily as an insertive partner. His last sexual contact was three-week-ago, unprotected with his friend. Serological tests showed an RPR titer of 1:8 and a positive TPHA indicative of syphilis infection. His partner was screened and found to have a healing ulcer over the coronal sulcus. His RPR was 1:256, and TPHA was reactive. However, his HIV serology was non reactive. Both the patient and partner were treated with injection benzathine penicillin 2.4 million units. Discomfort subsided in 10 days, and the lesion subsided after three weeks.

Case 9

Paraphimosis and balanitis: A 38-year-old male presented with erosions over the glans penis and paraphimosis persisting for one week [Table/Fig-9]. The painless lesions on the glans were initially noticed 10 days before, but discomfort and pain started after paraphimosis developed. His last sexual contact was four-week-ago. Apart from very mild hyperpigmented macules on the palms and soles, his skin examination was normal. Lymph node examination showed bilateral non tender inguinal adenopathy. He had no history of diabetes mellitus, and other causes of balanitis were ruled out. Upon inquiry, he reported multiple unprotected heterosexual activities with unknown partners over the past 16 years. Serological tests revealed an RPR titer of 1:64 and a positive TPHA indicative of syphilis infection. Additionally, his HIV serology was reactive. He received three doses of injection benzathine penicillin 2.4 million units. Oedema and paraphimosis slowly reduced after three days, and the pain subsided. The lesion on the glans healed in two weeks. The patient was referred to start ART. Follow-up RPR was 1:2 after eight weeks.



[Table/Fig-8]: Cord like thickening.



[Table/Fig-9]: Paraphimosis and Balanitis.

[Table/Fig-10] summarises all the nine cases with all clinical presentation and diagnostic details.

DISCUSSION

Syphilis is a preventable disease that, when timely diagnosed in the early stages, can be treated and transmission can be decreased. As a great imitator due to its protean presentations, it can mimic a number of common and rare diseases. Nine cases of syphilis have been reported that presented with atypical clinical manifestations. Of the nine cases, five individuals were identified as homosexuals, four had concomitant HIV infections, and all of them had used self-medication, either topically or systemically.

Case	Age/Sex	Clinical presentation	Sexual history	Antibiotics use	RPR	TPHA	HIV
1	57/M	Ulcer of lip mimicking squamous cell carcinoma with unilateral lymphadenopathy	Homosexual receptive and insertive role oral sex	Yes	1:64	Reactive	Non reactive
2	25/M	Crusted ulcer on areola mimicking ecthyma	Homosexual receptive role	Yes	1:16	Reactive	Non reactive
3	42/M	Lymphadenitis with sinus	Multiple heterosexual contact unknown partners	Yes	1:2	Reactive	Non reactive
4	28/M	Hyperkeratotic scaly plaques rembling psoriasis	Homosexual receptive and insertive roles	Yes	1:128	Reactive	Reactive
5	37/M	Scrotal eczema	Mutiple heterosexual contacts	Yes	1:8	Reactive	Reactive
6	26/M	Non indurated annular plaques resembling genital psoriasis/lichen planus	Homosexual contacts	Yes	1:32	Reactive	Non reactive
7	24/F	Multiple painful superficial ulcers- herpetic	Denied history	Yes	1:32	Reactive	Reactive
8	25/M	Cord like thickening	Homosexual contacts	Yes	1:8	Reactive	Non reactive
9	38/m	Paraphimosis	Unprotected heterosexual contacts	Yes	1:64	Reactive	Reactive

[Table/Fig-10]: Case summary.

The widespread use of broad-spectrum antibiotics for various ailments and self-medication practices has indeed modified the classical presentation of syphilis, making its diagnosis more challenging. Additionally, co-infection with HIV further modifies the clinical picture, adding ambiguity to the diagnosis of syphilis [3,4]. In all these patients, dark-field microscopy was done and found to be negative. Despite negative results from dark-field microscopy in all patients, reactive results were obtained for RPR and TPHA tests.

Extragenital chancres account for about 5 to 10% of syphilis cases [5]. The oral cavity is the most common region for these chancres, with the lip being the most frequently affected site in cases of oral primary syphilis [6]. Among men, the upper lip is reported to be the most common site, while the lower lip is more commonly affected in women, possibly due to practices such as fellatio and cunnilingus. A similar case of a syphilitic chancre of the lower lip was reported by Ni Y et al., in which a 24-year-old male patient with an ulceration of the lower lip was initially treated with mupirocin ointment and acyclovir ointment. When he disclosed a sexual contact two months prior, laboratory investigations were conducted, and he was diagnosed with syphilis [7]. In case 1 patient was initially suspected of carcinoma of the lip because of his age and was scheduled for surgical excision. He was later found to have an extragenital chancre of the lower lip. He responded well to penicillin treatment without undergoing any surgical procedures.

The nipple is also a common site for extragenital chancres, as seen in case 2 patient. There have been several reports of primary syphilis occurring on the nipple with varying clinical manifestations [6,8,9], such as erythema nodules on the nipple, swelling, erosion, indolent ulcers, asymptomatic scaly erythematous, or crusted plaque simulating Paget's disease. Other rare locations of extragenital chancres have been reported to include the hands, arms, chest, breasts, abdomen, legs, and feet [10]. Both the patients with extragenital chancres were found to be homosexuals with high-risk sexual practices.

Palmoplantar syphilis is commonly misdiagnosed as palmoplantar psoriasis. In a study by Solak B et al., the patient was treated for two years before the correct diagnosis was made [11]. In another study by Senthil Kumar V et al., the co-existence of psoriasis and palmoplantar syphilis was reported in a 38-year-old male who was also HIV reactive [12]. Given the high-risk sexual history and the clinical picture suggestive of syphilitic cornea, the patient was diagnosed with the help of laboratory tests and treated accordingly.

Scrotal eczema-like lesions were reported as the predominant and earliest manifestation of secondary syphilis in a study by Bains A and Tyagi N [13]. Additionally, two patients with secondary syphilis who presented with scrotal eczema were reported by Jeong E et al., [14]. In these patients, other skin lesions of secondary syphilis and palmar lesions were noticed during further follow-up, and lab investigations confirmed the diagnosis. But in Indian patients, slightly pigmented macules over palms and soles can be easily missed. Therefore, syphilis must be considered an important differential diagnosis in patients presenting with atypical scrotal lesions, as in present patient.

Annular secondary syphilis is a less common type of secondary syphilis, the prevalence of which is approximately 5.7-13.6% [15]. As in case 6, who presented with annular plaques resembling genital psoriasis or lichen planus, two cases of secondary syphilis with annular lichenoid plaques were reported in a study by Narang T et al., [16]. In these cases, the lesions cleared with a single dose of injection benzathine penicillin. Similarly, a case was reported in a study by Cai-Chou Z et al., where annular lesions on the penis were first treated as a fungal infection as this 21-year-old male complained of itching [17]. Fungal scraping was negative, and with the help of laboratory investigation, the correct diagnosis was made, and he was treated with injection benzathine penicillin.

Partner screening helped confirm the suspicion of syphilitic lesions in the female patient (Case 7) who presented with multiple ulcerations not responding to acyclovir and who was also HIV reactive. Laboratory investigations confirmed both syphilis and HIV positivity in her husband. Both individuals received three doses of injection benzathine penicillin.

Similarly, partner screening helped in making the diagnosis in the 25-year-old male (case 8) homosexual patient who presented with cord-like thickening on the dorsal aspect of the penis. His last contact was three-week-ago, and his partner had a healing ulcer in the coronal sulcus, and his RPR was 1:256 with a positive TPHA. Both were treated with injection benzathine penicillin. Partner screening helped confirm the diagnosis and ensure appropriate treatment for both individuals, preventing further transmission and complications. A case of penile Mondor's disease has been reported as a presentation of primary syphilis [18]. In a study by Sardinha JC et al., 25 patients with hardened lesions, in an arciform disposition 19 patients had a recent clinical and laboratory diagnosis of syphilis [19]. It was also emphasised that all patients who present with cord-like lesions on the penis must undergo a rapid test for syphilis, Venereal Disease Research Laboratory (VDRL), serologies for HIV viral hepatitis B and C, and, whenever possible, histopathological and Doppler exams [19].

In the literature, there are multiple case reports of secondary syphilis presenting as penile oedema, phimosis, paraphimosis, or indurative oedema of the prepuce mimicking phimosis [20,21]. Patient in the present series presented with balanitis and paraphimosis with non tender bilateral lymphadenopathy. His HIV serology was reactive. Based on the patient's history of unprotected sexual behaviours, clinical manifestations, and serological findings, he was diagnosed with syphilis. The patient received intramuscular benzathine penicillin G at a dose of 2.4 million units per week for three weeks. Early recognition of syphilis is critical because untreated syphilis not only leads to severe complications in the affected individual but also poses

a risk of transmission to others, contributing to the ongoing spread of infection. Thus, one must maintain a high- index of suspicion of syphilis, especially in individuals with high-risk sexual behaviour presenting with atypical lesions and HIV co-infection. Overall, heightened awareness, diligent clinical evaluation, and appropriate serological testing are crucial in overcoming the diagnostic challenges posed by atypical presentations of syphilis. Timely intervention will play a great role in mitigating the impact on both the individual and society. Thus, the purpose of this case series was to highlight the rare and confounding clinical manifestations of syphilis that can be missed if not suspected.

CONCLUSION(S)

Given syphilis's uniqueness as a great imitator and its chronic nature, a high-index of suspicion is crucial, especially with the increasing prevalence among high-risk individuals and complex presentations with co-existent HIV infection and inadvertent antibiotic usage. Early diagnosis is of paramount importance in any case of syphilis. Timely initiation of effective treatment with penicillin not only ensures complete cure but also halts the progression to severe forms of late syphilis. Awareness of these atypical manifestations among healthcare professionals will lead to heightened vigilance and effective management of cases of syphilis.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 02, 2024
- Manual Googling: Jun 12, 2024
- iThenticate Software: Aug 19, 2024 (13%)

ETYMOLOGY: Author Origin

EMENDATIONS: 5

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **May 02, 2024**
Date of Peer Review: **Jun 10, 2024**
Date of Acceptance: **Aug 20, 2024**
Date of Publishing: **Sep 01, 2024**